Remarks

In view of the above amendments and the following remarks, reconsideration of the outstanding office action is respectfully requested.

Claims 1-3, 6, and 26-28 have been amended. The independent claims have been amended to recite that the administration is carried out under conditions effective to achieve the recited effect (to treat or prevent atherosclerosis, as in claim 1; to prevent or treat atherosclerosis, as in claim 26; and to prevent development of atherosclerotic lesions, as in claims 27 and 28). Descriptive support for these amendments appears, *inter alia*, in the claims as originally filed and in the examples of the present application. Descriptive support for the amendment to claim 2 is provided at page 5, lines 16 to 17, of the present application. Therefore, no new matter has been introduced to the application. Claims 1-3, 6, and 26-28 remain pending.

The objection to application, and particularly claim 6, for non-compliance with the Sequence Listing requirements is respectfully traversed in view of the amendments to the specification and claim 6 to refer to the respective SEQ ID NOS: listed in the Sequence Listing. These objections should be withdrawn.

The rejection of claims 2 and 3 under 35 U.S.C. § 112 (second paragraph) for indefiniteness is respectfully traversed in view of the amendments to claims 2 and 3.

The rejection of claims 26-28 under 35 U.S.C. § 112 (first paragraph) for lack of written descriptive support is respectfully traversed.

On pages 4-6 of the outstanding office action, the U.S. Patent and Trademark Office ("PTO") asserts that the present application fails to provide descriptive support for the use of various classes of compounds recited in the presently claimed invention. Applicants disagree, because the specification identifies (i) a number of previously known GHRPs by citation to 18 prior art references on page 9, lines 5-15; and (ii) the members of the Hexarelin family and its derivatives (as GHRPs) on page 9, lines 17-23, two of which are identified and whose use is described in the examples; and (iii) peptides and peptidomimetic compounds that are GHRPs, as identified on page 8, line 27, to page 9, line 5. Moreover, the examples clearly correlate the observed effects of the GHRPs with negative modulation of CD36 expression and/or function, and increased mRNA levels of the LXRα and ABCA1 transporter

in macrophages. Therefore, persons of skill in the art would be fully aware of the various compounds that can be used to treat or prevent the recited conditions using known compounds within the recited classes.

For these reasons, the rejection of claims 26-28 for lack of written descriptive support should be withdrawn.

The rejection of claims 1-3, 6, and 26-28 under 35 U.S.C. § 102(a) as anticipated by Broglio et al., "Effects of Acute Hexarelin Administration on Cardiac Performance in Patients with Coronary Artery Disease During By-pass Surgery," *Eur. J. Pharmacol.* 448:193-200 (2002) ("Broglio") is respectfully traversed.

Broglio discloses the use of an acute dose of hexarelin on a patient (who has coronary artery disease) during by-pass surgery. Broglio reports that hexarelin improved cardiac function during the surgery. However, there is absolutely no disclosure whatsoever in Broglio that hexarelin can be used to treat or prevent atherosclerosis.

The PTO asserts that Broglio teaches treatment and/or prophylaxis of atherosclerosis by administering hexarelin, because the patient population undergoing by-pass surgery had coronary artery lesions. Applicants disagree, because Broglio merely evidences the effect of an *acute* dose of hexarelin during by-pass surgery. There is no indication and, indeed, no asserted basis for concluding that the hexarelin administration described in Broglio was effective in treating or preventing atherosclerosis. The authors of Broglio certainly make no such conclusion, and there is likewise no suggestion in Broglio of using hexarelin in the manner presently claimed.

There is likewise no basis for asserting that the administration of hexarelin in the manner described in Broglio inherently treated or prevented atherosclerosis. To establish that a reference inherently anticipates a claim, it must be demonstrated that the reference *necessarily* functions in accordance with the limitations of a claim. *See In re Cruciferous Sprout Litigation v. Sunrise Farms*, 301 F.3d 1343, 1349 (Fed. Cir. 2002). The PTO has asserted that Broglio discloses the same active step of administering hexarelin to "an identical patient population." Even if, assuming *arguendo*, the patient population is identical (which applicants do not admit), there is still no basis for concluding that the claimed step of administering hexarelin is the same as that disclosed in Broglio. That is because the single dose of hexarelin described by Broglio would not necessarily achieve effective results (i.e., an effective treatment of pre-existing atherosclerosis or a prophylaxis thereof). The present application provides evidence that repeated daily dosage, on the other hand, is effective.

Finally, it is a well established basis of patent law that new uses of known processes are patentable. *See* 35 U.S.C. § 101 (2004) ("Whoever invents or discovers any new and useful process … may obtain a patent therefore…."); 35 U.S.C. § 100(b) (2008) ("The term 'process' means process, art or method, and includes a new use of a known process, machine, manufacture, composition of matter, or material."). Whether or not a new use of a known process is patentable depends on whether or not the known process is "directed *to the same purpose*" as previously known processes. *See Bristol-Myers Squibb Co. v. Ben Venue Labs, Inc.*, 246 F.3d 1368, 1376, 58 USPQ2d 1508, 1514 (Fed. Cir. 2001) (emphasis added). In *Bristol-Myers*, the Federal Circuit held that claims directed to methods of treating patients for taxol-sensitive tumors by administering a certain dosage of taxol to a patient over about three hours, either with or without pretreatment of the patient for reduction of hypersensitivity to taxol, were inherently taught by a reference that reported phase I testing of taxol, using dosages and time constraints as claimed, and suggested pretreatment of patients to reduce their hypersensitivity. Importantly, the court noted that the claimed methods were *for the same purpose* as the known process described in the prior art (*id.*), and the claimed methods did not require a particular result of the recited steps (246 F.3d at 1372-73, 1378; 58 USPQ2d at 1514, 1515).

Therefore, even if the presently claimed process is the same as the process described in Broglio (which, for the reasons noted above, applicants do not admit), then a new use of the same process remains patentable where the purpose of the process is different. Unlike the single dose of hexarelin to promote cardiac performance during by-pass surgery, the presently claimed invention relates to an entirely different purpose: treating or preventing atherosclerosis (i.e., as recited in claims 1-3, 6, and 26) or preventing the development of atherosclerotic lesions (i.e., as recited in claims 27 and 28). Thus, this entirely different purpose clearly constitutes a new use, even if the claimed process of administering hexarelin constitutes a known process (which, for the reasons noted above, applicants submit it does not).

For all these reasons, the rejection of claims 1-3, 6, and 26-28 as anticipated by Broglio is improper and should be withdrawn.

The rejection of claims 1-3, 6, and 26-28 under 35 U.S.C. § 102(b) as anticipated by Imbimbo et al., "Growth Hormone-releasing Activity of Hexarelin in Humans," *Eur. J. Clin. Pharmacol.* 46:421-425 (1994) ("Imbimbo"), as evidenced by the AHA Heart and Stroke Statistics 2002 Update ("AHA 2002 report"), is respectfully traversed.

Imbimbo reports on the pharmacodynamic, safety, and tolerability results of hexarelin administration to healthy male subjects. Hexarelin was administered in three separate intravenous doses, with a randomly inserted placebo dose; and all injections were separated by "one-week washout periods" (*see* Imbimbo, *study design*). While Imbimbo notes that hexarelin administration can be used "in the diagnosis of GH deficiency and in the treatment of patients with insufficient somatotropic secretion due to hypothalamic dysfunction," Imbimbo does not disclose or suggest that hexarelin can be used to treat or prevent atherosclerosis.

The PTO has cited the AHA 2002 report as evidence that 90% of the (American) population has at least one risk factor for cardiovascular disease. However, there is no suggestion or disclosure that the at least one risk factor would inevitably lead to atherosclerosis.

The PTO has taken the position that the Imbimbo must necessarily teach the presently claimed method of preventing atherosclerosis via hexarelin administration, because the AHA 2002 report would allow a person of skill in the art to reasonably assert that the 12 healthy male subjects who received the hexarelin in the Imbimbo study—presumably having at least one risk factor for cardiovascular disease—would have been treated prophylactically for atherosclerosis. Applicants disagree for several reasons.

Firstly, it is improper to infer that any of the male subjects of Imbimbo had any risk factors for atherosclerosis and, therefore, were treated prophylactically. There is no indication in Imbimbo or the AHA 2002 report that the 12 subjects of Imbimbo are necessarily members of the American population identified in the AHA 2002 report. If anything, the fact that the authors of Imbimbo are all European and are associated with one or more entities in Italy, England, and France instead suggests that the 12 subjects of Imbimbo do *not* belong to the same population identified in the AHA 2002 report. Even so, if there is a 10% chance that any one member of the population did not possess at least one risk factor, then it cannot be said that any subject of Imbimbo *necessarily* possessed at least one risk factor for atherosclerosis.

Secondly, even if, assuming *arguendo*, that the 12 subjects of Imbimbo had at least one risk factor for cardiovascular disease (which applicants do not admit), it is improper to conclude that the at least one risk factor—in the absence of the several limited doses of hexarelin—would inevitably lead to atherosclerosis.

There is likewise no basis for asserting that the administration of hexarelin in the manner described in Imbimbo inherently prevented atherosclerosis. That is because the limited doses of hexarelin—with extended 7 or 14 day "washout" periods—described by Imbimbo would not necessarily achieve effective results (i.e., an effective treatment of pre-existing atherosclerosis or a prophylaxis thereof). The present application provides evidence that repeated daily dosage, on the other hand, is effective.

Finally, for substantially the same reasons noted above with respect to the rejection over Broglio, applicants submit that the presently claimed process constitutes a patentable new use even if the process was previously known (which for the reasons noted above, it was not).

In view of all of the foregoing, applicants submit that this case is in condition for allowance and such allowance is earnestly solicited.

Respectfully submitted,

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